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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/019,441	02/05/1998	MITCHELL E. REFF	012712-502	2038

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[REDACTED] EXAMINER

JAMROZ, MARGARET E

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1644

DATE MAILED: 11/23/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)
	09/019,441	REFF ET AL.
	Examiner	Art Unit
	Margaret E Jamroz	1644

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) The period for reply expires _____ months from the mailing date of the final rejection.
- b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP-706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on 24 September 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. The proposed amendment(s) will not be entered because:
 - (a) they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) they raise the issue of new matter (see Note below);
 - (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. Applicant's reply has overcome the following rejection(s): _____.
4. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment.
6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none.

Claim(s) objected to: none.

Claim(s) rejected: 1,2,4,5,8-15,17,18 and 21-25.

Claim(s) withdrawn from consideration: 26-37.

8. The proposed drawing correction filed on _____ is a) approved or b) disapproved by the Examiner.
9. Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. Other: _____

Art Unit: 1644

DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating papers for this application, all further correspondence regarding this application should be directed to Megan Jamroz in Art Unit 1644, Technology Center 1600.

2. Claims 1, 2, 4, 5, 8, 9, 10-15, 17-18, and 21-25 are pending.

In view of the amendment filed on 24 September 2001 (Paper NO: 26), only the following rejections remain.

3. Claims 1, 2, 4, 5, 8, 9, 14, 15, 17, 18, 21, and 22 stand rejected under 35 U.S.C. 102(a) as being anticipated by Bonnefoy et al (WO 96/12741) as evidenced by Saxon et al. (J. Immunol, 1991. 147(11): 4000-4006) for the same reasons set forth in Paper NO: 25.

The applicant's position is that Bonnefoy does not teach anti-CD23 antibodies that have a human IgG1 or IgG3 constant region, and Saxon et al does not evidence that such antibodies inherently inhibit IgE expression. Applicant argues that Bonnefoy does not describe any specific chimeric or humanized antibody which inhibits IgE expression to a greater extent than the antibody without such constant region, only that antibodies may elicit a lesser immune response. Applicant also argues there is no guidance for the skilled artisan to pick any of the modified antibodies that would potentially inhibit IgE expression to a greater extent than the others.

The examiner's position is the same as set forth in Paper NO: 25. The Bonnefoy et al. reference teaches a anti-CD23 antibody (monoclonal, humanized, primatised, fragments, and pharmaceutical compositions) that is either IgG1 or IgG3, and a rodent antigen binding domain that binding agents to CD23 can be of utility in the treatment of allergic diseases (e.g. inhibit IgE expression) (see page 3, paragraphs 2-6; page 4, paragraphs 4 and 5; page 5, paragraphs 1, 2 and 5; and page 6, paragraph 1). The Saxon et al reference teaches the inherency for anti-CD23 antibodies to inhibit IgE expression using an IgG1 monoclonal antibody against CD23 (of record in Paper NO: 25).

It is applicant's further view that Bonnefoy et al. is more appropriately applied as a 103(a) reference and that the gamma-1 surprising results are unexpected.

Examiner disagrees and maintains that Bonnefoy et al. teaches supra and is correctly applied as a 102(a) reference as evidenced by Saxon et al. Therefore, applicant's arguments regarding Bonnefoy et al. are not considered persuasive and the 102(a) rejection stands.

4. Claims 1-2, 4-5, 8-11, 14-15, 17-18, and 21-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Queen et al. (U.S. Patent 5,385,089), of record, in view of Saxon et al., of record, for the same reasons set forth in Paper Nos: 13 and 24.

Applicant's position is that the '089 patent and Saxon et al. reference were disregarded in the parent application, and therefore call into question the validity of U.S. Patent 6,011, 138.

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It is the examiner's position that the rejection was vacated solely because of the Wakai et al. reference in the parent case, and not over Queen et al. in view of Saxon et al. See section 6 in Paper No: 24. Therefore, applicant's arguments regarding Queen et al. in view of Saxon et al. are not considered persuasive.

5. Claims 1, 2, 5, 8-9, 14-15, 17-18, and 21-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Newman et al (U.S. Patent 5,658,570) as evidenced by Saxon et al. (J. Immunol, 1991. 147(11): 4000-4006) for the same reasons set forth in Paper NO: 25.

The applicant's position is Newman does not disclose an anti-CD23 antibody having a gamma-1 constant region, that it would have been *prima facie* obvious to substitute the gamma-1 region used in the anti-CD4 antibody disclosed or that the '570 patent did not provide any motivation to choose gamma-1 constant domains over any other gamma constant region (or any other antibody isotype) or that anti-CD23 antibodies are useful for inhibiting IgE production.

The examiner's position is the same as set forth in Paper NO: 25. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and not is it that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Once a *prima facie* case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). Applicant's reliance on unexpected results do not overcome clear and convincing evidence of obviousness. Also see Richardson-Vicks Inc. v. Upjohn Co., 44 USPQ2d 1181 (CAFC 1997). In considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968).

Thus, even though the '570 does not address anti-CD23 antibodies useful for inhibiting IgE production, antibody effector function playing a specific role in that activity, or choosing gamma-1 constant domains over any other constant region or antibody isotype, the '570 patent encompasses recombinant antibodies for human therapy, wherein the chimeric antibody comprised an immunoglobulin constant region (e.g. humanized or primatized) and an antigen binding region (e.g. Old World Monkey) wherein the antibody binds specifically to a human antigen (e.g. CD23; see claims 1-8 in particular). The '570 patent also claims chimeric recombinant antibodies wherein the human constant region was human gamma-1 (see claim 35 in particular). Thus, it would have been well within the purview of one of ordinary skill in the art at the time the invention was made to design humanized gamma-1 or gamma-3 antibodies against human CD23 to inhibit IgE production or for use as therapy in humans. The combined '570 patent and Saxon et al references teach the inhibition of IgE production with humanized, chimeric, or primatized anti-CD23

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antibodies, providing a motivation for the instant application as well as a reasonable expectation of success.

Applicant argues that although Newman was not cited during the prosecution of the '138 patent, the '570 patent implicitly challenges the validity of the '138 patent.

It is the examiner's position that each reference must be considered individually. It is well settled that whether similar claims have been allowed to others is immaterial. See *In re Giolito*, 530 F.2d 397, 188 USPQ 645 (CCPA 1976) and *Ex parte Balzarini* 21 USPQ2d 1892, 1897 (BPAI 1991).

6. Claims 1, 2, 4-5, 8-15, 17-18, and 21-25 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of co-pending Application No. 09/292,053. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the same reasons set forth in Paper NO: 25. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's request in amendment filed 2/7/01 to hold this rejection in abeyance is noted. However, until a terminal disclaimer is filed, the rejection stands.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Margaret (Megan) Jamroz, Ph.D.
Patent Examiner
Technology Center 1600
November 15, 2001

Christina Chan
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